IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:	)	Art Unit: 1647
NIELSEN, et al.	)	Examiner: DEBERRY, REGINA
Serial No: 09/845,716	)	Washington, D.C.
Filed: May 2, 2001	)	
For: USE OF α-MSH AND EPO FOR PREVENTING OR TREATING ISCHEMIC CONDITIONS	)	Docket No.: NIELSEN=3A
	)	Confirmation No.: 3819

DECLARATION OF THOMAS JONASSEN

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I hereby declare:

1. I am one of the inventors of the above-identified patent application.
2. I am a M.D. and Associate Professor in Cardiovascular and Renal Pharmacology at the University of Copenhagen. My curriculum vitae is attached.
3. I am an employee of ACTION PHARMA A/S and I presently hold the position of Chief Scientific Officer.
4. I have studied the references cited by the examiner. Shohaib et al. describes the use of EPO in the treatment of anamia in a post-renal transplant patient. The anaemia is not due to renal failure. The reference mentions a woman who has chronic renal failure and receives a renal transplant. After the renal transplantation her serum creatinine clearance is measured several times and is 50 ml/min and 60 ml/min, respectively (p.82, column 1, 2nd paragraph, line 8, 22-23, 33). A creatinine level of 50 ml/min or 60 ml/min is considered indicative for normal function of a transplanted kidney and the woman is therefore not suffering from chronic renal failure. This is further supported by the author's comment on her graft function of the transplanted kidney

p.82, column 2, 2nd paragraph, lines 2-4: "her graft function was satisfactory and could not account for her anaemia". Thus, Shohaib et al. teaches the use of EPO in the treatment of anaemia and not renal failure.

Kwon et al. describes that α-MSH treatment reduces downregulation of renal aquaporins and reduces polyuria in rats with ischemia-induced acute renal failure. In more details, Kwon et al. examines the effect of temporary renal ischemia and reperfusion on the expression of renal aquaporins and urinary concentration in rats with bilateral ischemia-induced acute renal failure. Subsequently, they test whether reducing ischemia/reperfusion injury by treatment with α-MSH affects the expression of aquaporins and urine output (page F413, column 1, lines 10-12). They find that α-MSH treatment reduces the expression of aquaporins and also reduces urine output (page F413, column 1, lines 34-36). Thus, Kwon et al. teaches that α-MSH treatment of rats with acute renal failure results in a reduced ischemia-induced downregulation of renal aquaporins and in a reduced polyuria. This is not the same as teaching the use of α-MSH for the treatment of anaemia. Importantly, anaemia is not observed in acute renal failure. It could therefore be argued that Shohaib et al. and Kwon et al. do not teach the use of EPO and α-MSH, respectively, for the same purpose and thus, that it is not obvious to combine EPO and α-MSH in a composition.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 11/5-2005

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CURRICULUM VITAE

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Clinical training 1995-97 at Kalundborg Sygehus and Herlev University Hospital.

Position 1993. Pregraduate Research Fellow at the Department of Pharmacology, University of Copenhagen.
1995-1996. Recidency at Kalundborg Sygehus
1996-1998. Research Fellow, Department of Pharmacology, University of Copenhagen.
1998-2000. Assistant Professor, Department of Pharmacology, University of Copenhagen
2000-present. Associate Professor, Department of Pharmacology, University of Copenhagen
2004-present. Chief Scientific Officer, Action Pharma (part time)

Research Interests Research focus on integrative pharmacology/pathophysiology with special focus on renal dysfunction in congestive heart failure and liver cirrhosis. Additional focus on pulmonary microvascular permeability and alveolar fluid resolution in Congestive heart failure.

Supervision Supervisor for 4 Ph.D. students that have completed their thesis (all at the University of Copenhagen). Currently supervisor for 4 Ph.D. students (at the University of Copenhagen).

Publications 26 original papers (all in international journals) and 3 patents.

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Professor Peter Deen, PhD, Nijmegen, The Netherlands
Professor Gerald DiBona, MD, Iowa City, Iowa, USA

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Ten selected publications

1. Jonassen, T.E.N., N. Marcussen, K. Haugan, H. Skyum, S. Christensen, F. Andreasen, and J.S. Petersen: Functional and structural changes in the thick ascending limb of Henle´s loop in rats with liver cirrhosis. Am. J. Physiol. Regulatory and Integrative Physiol. 273: R568-R577. 1997.

2. Jonassen, T.E.N., S. Nielsen, S. Christensen, and J.S. Petersen: Decreased vasopressin-mediated renal water reabsorption in rats with compensated liver cirrhosis. Am. J. Physiol. Renal Physiol. 275: F216-F225, 1998.

3. Jonassen, T.E.N., S. Christensen, N. Marcussen, A.-M- Sørensen, A. Flyvbjerg, F. Andreasen, and J.S. Petersen. Effects of chronic octreotide treatment on renal changes during compensated liver cirrhosis in rats. Hepatology 29:1387-95, 1999.

4. Jonassen, T.E.N., D. Promeneur, S. Christensen, J.S. Petersen, and S. Nielsen. Decreased vasopressin-mediated renal water reabsorption in rats with chronic aldosterone-receptor blockade. Am. J. Physiol. Renal Physiol. 278: F246-F256, 2000.

5. Jonassen T.E.N., S. Christensen, Tae-Hwan Kwon, S. Langhoff, N. Salling, and S. Nielsen: Renal water handling in rats with decompensated liver cirrhosis. Am. J. Physiol. 279: F1101-F1109, 2000.

6. Staahltoft D., S. Nielsen, N.R. Janjua, S. Christensen, N. Marcussen, O. Skøtt and T.E.N. Jonassen: Chronic losartan treatment normalizes renal water handling in rats with congestive heart failure. Am. J. Physiol. Renal Physiol. 282: F307-F315, 2002

7. Jonassen T.E.N., L. Brønd, M. Torp, M. Græbe, S Nielsen, O Skøtt, N. Marcussen and S Christensen: Effects of renal denervation on thick ascending Na reabsorption in rats with liver cirrhosis. Am. J. Physiol. Renal Physiol. 284: F555-63, 2003

8. Græbe M., L Brønd, S Nielsen, S Christensen, NV Olsen and T.E.N. Jonassen: Chronic Nitric Oxide Synthase Inhibition Exacerbate Renal Dysfunction in Cirrhotic Rats. Am J Physiol Renal Physiol. 286:F288-97, 2004

9. Hadrup N, J.S. Petersen, J. Praetorius, E. Meier; M. Græbe; L. Brønd; D. Staahltoft; S. Nielsen, S. Christensen and T.E.N. Jonassen. Opioid receptor-like 1 stimulation in the collecting duct induces aquaresis through vasopressin-independent aquaporin-2 downregulation. Am J Physiol Renal Physiol. 287:F160-8, 2004

10. Brønd L., N. Salling, S. Christensen, S. Nielsen, M. Græbe and T.E.N. Jonassen: Uncoupling of vasopressin signaling in collecting ducts from rats with CBL induced liver cirrhosis. Am J Physiol Renal Physiol. 287:F806-15, 2004